

REMARKS

Claims 1-7, 9-29, 31-39 and 49-61 are pending. Applicants' undersigned attorneys wish to express their appreciation for the telephone interviews graciously provided by the Examiner on January 11th. Reconsideration and withdrawal of the rejections of the pending claims is respectfully requested in view of the following amendments and remarks which were made further to the understanding reached during those telephone interviews.

A. THE TELEPHONE INTERVIEWS

During the January 11th telephone discussions, the following points were believed to be agreed upon: (1) The Examiner will accept claim 1 as patentable, i.e., both supported by the specification and free of the cited art, if amended to recite that the polymer is a polyalkylene oxide having an alkyl-terminal, i.e., at least one polymer terminal is alkyl substituted or capped; and (2) the Examiner will accept claim 14 (reciting a Markush group of additional polymers that do not include polyalkylene oxides), as patentable if claim 14 is amended to be independent. Independent claims 15, 19 and 21 are amended analogously to claim 1.

B. THE AMENDED CLAIMS

Claim 1, 7, 9-10, 14-15, 19, 21, 27-28 and 31 are amended. Claims 1, 15, 19 and 21 are amended to recite that the substantially non-antigenic polymer forming the conjugate is a polyalkylene oxide comprising an alkyl-terminal. This amendment is supported by the specification, for example, lines 18 et seq. on page 7. Claim 14 is amended to be independent, without further limitation, to provide the same scope for this claim as was recited when claim 14 was dependent on claim 1, as originally filed. Claim 21 is also amended to recite that the polymer is selected from a Markush group as recited, which is supported for all of the reasons that claims 1 and 14 are supported. Claim 7 is amended to more clearly state that which Applicants consider to be their invention, and is supported by the specification, e.g., the paragraph bridging pages 9 and 10 of the specification. Claims 9, 10 and 31 are amended to avoid dependency on canceled claims 8 and 30, respectively. Claim 27 is also amended to change "molar" excess to "molar ratio" which, with other conforming language addresses the Examiner's rejection under 35 U.S.C. § 112, second paragraph, for this claim. The amendment to claim 27 is supported, e.g., at page 3,

lines 23-25 and page 9, lines 1-2, indicating that an equimolar ratio is contemplated. Since claim 27 is amended, the dependency of claim 28 is conformed.

C. THE NEW CLAIMS

The Application is amended to include additional claims that are believed to more fully set forth that which Applicants' consider to be their invention. Thus, new dependent claims 49-60 are provided to set forth the particulars of Applicants' invention, and are respectfully urged to be fully supported by the specification. New claims 49-57 are simply copied from claims dependent upon claim 1. New claim 54 is essentially analogous to claim 7 as discussed above. New claims 58-60 are dependent upon independent claims 1, 19 and 21, respectively and are supported by the specification, e.g., at page 8, lines 2-3, which states that, "[i]n addition to mPEG, C₁₋₄ alkyl-terminated polymers are also useful." New claim 61 is a product by process claim and it is respectfully urged that this claim is supported by the specification for all of the reasons that, e.g., claim 21 is supported by the specification.

D. THE OFFICE ACTION

At paragraph 1 of the Official Action, the Examiner has objected to the recitation of the word, "TWEEN" without uppercase lettering and without generic terminology, in the specification at page 16, line 27. The specification has now been amended to change all occurrences of "tween" to -- TWEEN® --. Otherwise, it is respectfully urged that the required generic description is already provided in the specification, as filed, at page 13, line 30 which describes, "materials such as polyoxyethylene sorbitans (Tweens)." This generic language and the correct trade name has now been copied to page 16, line 27, for consistency. For these reasons, it is respectfully urged that this ground of objection is now obviated. Therefore, the Examiner is respectfully requested to reconsider and withdraw this objection.

At paragraph 2 of the Official Action, the Examiner has objected to an alleged lack of support for the language of claims 40-48, added by Preliminary Amendment. As discussed during the telephone interviews, it is Applicants position that there is sufficient support for these claims in the parent application, now U.S. Patent No. 5,711,944, issued on January 27, 1998, and incorporated by reference into the instant patent application. Nevertheless, in the interest of expeditious prosecution, Applicants have canceled these claims without prejudice, while reserving the right to prosecute the subject matter of these claims in a subsequent continuation,

continuation-in-part or divisional patent application. For this reason, it is respectfully urged that this ground of objection is now obviated. Therefore, the Examiner is respectfully requested to reconsider and withdraw this objection.

At paragraph 3 of the Official Action, the Examiner has rejected claims 15-18, 27 and 37 as allegedly indefinite for lacking an antecedent basis for, "said substantially non-antigenic polymer." Claim 15 as amended corrects this informality, also obviating this ground of objection.

The Examiner has also rejected claim 27 for reciting a, "molar excess" but then reciting a numerical ratio ranging from about 1 to about 8. The Examiner's comments on claim 27 are appreciated, but it is believed that the best way to address this informality is to amend claim 27 to recite that, "wherein said polymer is present in a molar ratio ranging from about 1 to about 8-fold." An equimolar ratio of about 1 is supported by the specification at page 9, lines 1-4, which states that, "[t]he reaction conditions for effecting conjugation further include conducting the attachment reaction with from about equi-molar to about a relatively small molar excess of the activated polymer with respect to the alpha-interferon."

For all of these reasons, it is respectfully urged that all of the Section 112, second paragraph grounds of rejection are now obviated. Therefore, the Examiner is respectfully requested to reconsider and withdraw these rejections.

At paragraph 4 of the Official Action, the Examiner has objected to the specification for an alleged failure to provide "proper antecedent basis" for claims 40-48. The support for claims 40-48 has been addressed, above. However, since these claims have been canceled without prejudice, it is believed that this ground of objection is now obviated. Therefore, the Examiner is respectfully requested to reconsider and withdraw this objection.

At paragraphs 4 and 5 of the (revised) Official Action, the Examiner has objected to the claim of priority for the instant patent application, noting that both Greenwald et al. (U.S. Patent No.5,738,846) and European Patent Application 0 809 996, will therefore be available as art to be cited against the pending claims.

Applicants respectfully disagree with the Examiner's characterization of Applicants priority claim. Nevertheless in the interest of efficient prosecution, the Examiner's attention is also respectfully directed to the above-amended claims, which Applicants believe are distinguished from the art cited by the Examiner.

At paragraph 7, claims 1-9, 11-13, 15-27 and 30-39 are rejected under 35 U.S.C. § 102(e) as anticipated by Greenwald et al. Greenwald et al. fails to teach the claimed pharmaceutical compositions and methods wherein the substantially non-antigenic polymer is, "polyalkylene oxide comprising an alkyl terminal." The advantage of employing such a polyalkylene oxide comprising an alkyl terminal is that one terminus of the polymer is effectively capped, allowing for production of mono-conjugated interferon products. In contrast, Greenwald teaches compositions and methods utilizing uncapped polymers, which provide mixtures of both mono- and bis-conjugated polymer-interferon compositions. Further, it is respectfully submitted that Greenwald et al. fails to teach the compositions of claims 14 and 21 and the claims dependent thereon, directed to the Markush group of alternative polymers for use in preparing conjugates according to the invention.

For all of these reasons, it is respectfully urged that these grounds of rejection be reconsidered and withdrawn for all pending claims.

At paragraph 8, claims 40-48 are rejected under 35 U.S.C. § 102(e) as anticipated by Greenwald et al. Given the cancellation of these claims, this ground of rejection is obviated.

At paragraph 9, claims 40-48 are rejected under 35 U.S.C. § 102(a) as anticipated by European Patent Application '996. Given the cancellation of these claims, this ground of rejection is obviated and the Examiner is respectfully requested to reconsider and withdraw this rejection. It should also be noted, for the record, that the '996 reference teaches that the conjugation reaction be conducted under alkaline conditions and that acidification of the reaction mixture is desirable only for terminating the reaction. For this reason, it is believed that the '996 reference teaches away from Applicants' claimed invention.

At paragraph 10, claims 10, 14, 28 and 29 are objected to as being dependent upon a rejected base claim. Applicants respectfully disagree. Given the above-described amendments to the independent claims, it is respectfully urged that this ground of objection is therefore obviated and the Examiner is respectfully requested to reconsider and withdraw this rejection.

E. FEES

Applicants have enclosed herewith a check in the amount of \$146.00 for a Large Entity. This includes the fee of \$110.00 for the petition under 37 C.F.R. § 1.136 to extend the time to respond for one month, plus the \$36.00 fee for two additional total claims. Prior to the above claim amendments, the instant patent application had a total of 48 claims, with a total of 9

independent claims. After amendment, 11 total claims were canceled and 13 total new claims were added, for a total of 50 remaining claims. After amendment, 2 independent claims were canceled and two independent claims were added. Thus, it is believed that a fee is due only for two additional claims in excess of twenty, for a total fee of \$36.00 for extra claims.

Any deficiency or overpayment associated with this response should be charged or credited to Deposit Account No. 50-0217.

F. DRAWINGS

Applicants respectfully request that the submission of corrected drawings be delayed in accordance with the provisions of 37 C.F.R. 1.85 until a Notice of Allowability is received.

G. CONCLUSION

Applicants respectfully assert that they have obviated each and every one of the rejections and objections raised by the Examiner as a consequence of the action taken above. Accordingly, it is respectfully submitted that the pending claims are in condition for allowance. Reconsideration of the claims and early action to provide a Notice of Allowance is respectfully requested.

If the Examiner believes that an interview, either personal or telephonic, would advance the prosecution of this application, it is respectfully requested that he contact the undersigned.

Respectfully submitted,

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